

**FDA Virtual Town Hall Series –
Immediately in Effect Guidance on
Coronavirus (COVID-19) Diagnostic Tests**

**Moderator: Irene Aihie
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Coordinator: Good morning. Welcome everyone to today's conference call. At this time your lines have been placed on listen-only for today's conference until the question-and-answer portion of our call at which time you will be prompted to press Star 1 on your touch-tone phone. Please ensure that your line is on muted and please record your name when prompted to be introduced to ask your question. Our conference is being recorded and if you have any objections you may disconnect at this time. I will now turn the conference over to our host Ms. Irene Aihie. Ma'am you may proceed.

Irene Aihie: Thank you. Hello. I am Irene Aihie of CDRH's Office of Communication and Education. Welcome to the FDA's 44th in a series of virtual town hall meetings to help answer technical questions about the development and validation of tests on SARS-CoV-2 during the public health emergency.

Today Toby Lowe, Associate Director of the Office of In Vitro Diagnostics and Radiological Health and Timothy Stenzel, Director of the Office of In

Vitro Diagnostics and Radiological Health in the Office of Product Evaluation and Quality, both from CDRH, will provide a brief update.

Following opening remarks we will open the line for your questions related to the development and validation of tests for SARS-CoV-2. Please remember that during this town hall we are not able to respond to questions about specific submissions that might be under review. Now I give you Toby.

Toby Lowe: Thanks Irene and thanks everyone for joining us again this week. I have a couple of updates this afternoon. First as you may have seen on Monday we issued a new guidance document for the policy for evaluating impact of viral mutations on COVID-19 tests.

Obviously this is a topic that we've talked about here on the town hall quite a bit recently. And we now have this guidance document out that was put out along with a suite of guidance documents from the other centers as well on the same topic for different medical products.

So our guidance provides information on evaluating the potential impact of emerging and future viral genetic mutations on COVID-19 tests including design considerations and ongoing monitoring.

As you all know we've already issued a safety alert about this topic and identified a few tests that are known to be impacted though at this time that impact does not appear to be significant. We continue to monitor and will put out additional alerts as needed if and when future impacted tests are identified.

Now the guidance goes into the monitoring that FDA does as well as describing recommendations for test developers, such as considering the potential for future viral genetic mutations when designing your test,

conducting your own routine monitoring to evaluate the potential impact of new and emerging genetic mutations and information that we would expect to be provided to FDA on both in an EUA requests and in supplemental EUA requests or reports after authorization with ongoing monitoring.

And it does provide more detailed recommendations for developers of molecular CoV-2 tests and also discusses the sort of landscape of monitoring for antigen and serology as far as SARS-CoV-2 tests and forecasts that we will put additional information regarding that monitoring in the EUA templates as more details are worked out.

So that guidance can be found on our Web site and if there are any questions we're happy to take them on the call today or you can also send a questions to the mailbox as you're all familiar with.

The other topic that I wanted to bring up before we get into the questions is to clarify some comments that were made last week regarding usability test - usability and user comprehension studies. One of the risks of a town hall forum like this is that Tim and I don't always have the source documents open in front of us, so we don't always have all of the details to best answer the questions that come up. So sometimes we like to do a little research and come back and clarify for everyone.

So we had a question last week about questionnaires following usability studies and there may have been some confusion between usability studies and user comprehension studies. So we want to clarify that those are two different things, that they're different purposes and provide different validation information.

Usability studies assess whether the intended user of the device can use the device properly without serious use errors or problems. And this testing typically would include an observational specimen of the users performing the testing, an assessment of the sample collected or the testing performed by the intended user and an interviewer questionnaire to assess the users' perspectives on the usability of the device.

Our current template for molecular and antigen diagnostic tests for tests outside of healthcare settings the - and we refer to it as the non-lab or the home use test - or sorry template, does include a recommendation to assess the users' perspective on the usability of the device using a questionnaire consistent with the recommendations and our 2016 human factors guidance.

I will note that the question last week referred to that 2016 human factors guidance. And I do want to point out that some of the details in that guidance while they are, the general concepts are applicable to IVDs, the - there are specific details that are necessary to consider for IVDs since the guidance document is written for evaluating user interfaces which is different from evaluating an IVD where that involves collecting a sample and performing a test as opposed to simply interfacing with a user interface.

So that's - those are usability studies. And then separate from usability studies there are user comprehension studies. User comprehension studies are intended to objectively assess the intended users' understanding or comprehension of critical elements and concepts in the labeling. These studies are particularly important for tests that are intended for use by the users that do not include the involvement of a healthcare provider.

The current template for non-lab tests does not discuss user comprehension studies but we do think that this is very important to assess especially for tests

where there's not healthcare provider involvement to consider user comprehension and assess the comprehension of labeling for devices where the results are returned to the lay user.

And I want to note particularly for serology tests -- and we are currently working on a template to provide recommendations for validation for serology tests performed outside of healthcare settings, there are significant risks associated with lay user misinterpretation and misuse of serology tests since they should not be used to diagnose acute infection and its unknown whether antibodies confirm immunity or protection from infection and if so how long that may last.

The clinical significance of serology test results especially in individuals that have received vaccine is unknown. So given the current limitations of serology testing, lay users may misunderstand and potentially misuse serology test results. So it's particularly important to assess the users understanding of the test including its limitation.

So with that clarification of that discussion from last week I - that concludes my update and I don't think Tim has any further updates this week so...

Dr. Timothy Stenzel: Yes Toby...

Toby Lowe: Yes?

Dr. Timothy Stenzel: ...can you hear me? Yes I just wanted...

Toby Lowe: Yes.

Dr. Timothy Stenzel: ...to update one thing. That I just want to reemphasize our current priorities for review at the FDA for tests. So obviously home over-the-counter tests including rapid antigen tests are a high priority as well as home prescription tests including rapid antigen tests. Also a point of care test including rapid antigen tests as well as extremely high throughput central lab tests pretty much of any sort. We're really looking for both molecular and antigen, the diagnostic test for the high throughput systems. So with that Toby and operator I think we can go to our questions, the question period. Thank you.

Coordinator: Thank you. At this time if you would like to ask a question please press Star 1 on your touch-tone phone. Please ensure that your line is unmuted and please record your name when prompted to be introduced.

Once again it is Star 1 at this time. Our first question is from Ariana Perez. Your line is open.

Ariana Perez: Hi. My name is Ariana. I'm with UserWise. I have a question. Is an anterior nasal swab with no stopper allowable for use with children under 14 in an OTC context or does the FDA have data suggesting that nasal swabs with no stopper are unsafe for children under 14 even for anterior nasal swabs?

Dr. Timothy Stenzel: So we're interested in safety in the home environment and especially when untrained non-healthcare people are doing swabbing at home. So for an anterior nasal swab it's clearly shown and in the study shows there's no harm done, that's good.

If you're going to go further in than an anterior nasal swab such as a mid-turbinate swab that's at the point that we would like some sort of safety

features. And certainly we encourage developers to even for anterior nasal swabs to think about safety in that situation.

Ariana Perez: Okay so for anterior nasal swabs it's acceptable to not have a stopper but FDA is requesting stoppers for mid-turbinate swabs?

Dr. Timothy Stenzel: A stopper would be ideal. There are potential other mediations on the different sort of swabs with, you know, some sort of adapter that some developers have used, but something yes to make sure that the children are safe when they're getting swabbed.

Ariana Perez: Okay thank you.

Coordinator: Thank you. Our next question is from (Dee Dee Datra). Your line is open.

(Dee Dee Datra): Hi. So I - my question is related to the new guidance that was issued about the impact of wider mutation. So the first part of my question is can you please recommend a source for obtaining specimens positive for these mutations? And the second part is, is there any guidance that we can get on how to evaluate the performance of the test? And so because we are developing a serology test for the point of care use and we're intending to submit the EUAs pretty soon.

Dr. Timothy Stenzel: So for serology tests there's, you know, current thinking is there's, you know, some things that we can do. For example every serology developer would know the epitope that's of the virus that's being used. They know the sequence of amino acids. So you can check the known public databases for any prevalence mutations that impact the new assay sequence of your epitope in your assay.

Only if it does impact directly your epitope or if you have the means of assessing whether it's amino acid change outside the epitope could impact things. But I think, you know, right now the best way to go about this is to look at that epitope antigen that you're using in your assay and make sure there aren't any prevalent.

And we usually use the 5% rule but check out the guidance 5% or below or 5% in total or below or it doesn't push the performance for the assay down below what we would usually expect to see for authorization.

And obviously if you do have an epitope that has a prevalent mutation that leads to an amino acid change, you'll want to assess what the potential impact on that amino acid change is. Is it something - is it, you know, something shouldn't actually change too much, you know, it may be a very similar, you know, amino acid. But in all likelihood if it's changing amino acid, it may be due to immune function that may allow it to somewhat evade the patient's immune system.

And so then how do you know beyond that for serology tests if it impacts? And that would probably involve trying to find immune serum or plasma by from a patient who carries that mutation or variant in order to assess that.

But again it's all risk-based, so if that mutation or variant is less prevalent right now we may just authorize the test with labeling that says, you know, there's a potential, you know, problem with this mutation or with this assay. But hopefully that's helpful enough and we hope, you know, that that immune serum will be available to developers. And, you know, we're certainly thinking about all of those things. so but I don't have any program to announce right now other than what I've just talked about as far as looking at amino acid changes in the serology epitope molecule.

(Dee Dee Datra): Okay thank you. But just to clarify so is the - can FDA recommend a source that we obtain specimens that may be positive for the most prevalent mutations right now?

Dr. Timothy Stenzel: Yes it would be in the case of serology tests it would be immune plasma or serum from a patient known to have been exposed by the virus that could - genotype that could impact your assay. So that's obviously going to be a challenging sample for anybody to accumulate. So we're certainly in the process of looking into that. but I have no solution. I have no recommendation at this point unfortunately.

(Dee Dee Datra): Okay. Thank you so much.

Coordinator: Thank you. Our next question's from (Vana Smith). Your line is open.

(Vana Smith): Thank you. Tim, first thanks to all the reviewers for all their hard work. And I wanted to go back to January when you did an update on the MDUFA hold or backlog since we were all - many of us were interested in both MDUFA submissions and EUA. I was wondering if you could give an update?

Dr. Timothy Stenzel: Yes so just for those that don't know because of the volume of COVID applications all applications in total for COVID, you know, including pre-EUA, original UAs, EUA supplement amendments we're seeing somewhere between 200 and 300 new applications a month still. And that's just a tremendous volume but obviously it has great importance for the country.

And as a result we did move headcount from non-COVID work to COVID work and in the process took people off of regular MDUFA non-COVID

work. And as a result we, you know, because of the work load volume we did put files on hold.

And those holds, I was going to say, are not indefinite. They will come to a very specific end, no matter what file. So and all files will be treated equally and they - this is not an indefinite hold and we will be communicating that with each sponsor.

So if we can't get back to it on the first hold, the next communication will spell out exactly when we can get back to that file. And so it will not go on indefinitely. Hopefully that addressed your question.

(Vana Smith): Yes thank you.

Coordinator: Thank you. Our next question is from (Joann Gonzales). Your line is open.

(Joann Gonzales): Thank you for taking my question. Has the agency authorized any mobile medical applications either for COVID-19 or otherwise that are supported on both iOS and Android. And if so, were there any specific requirements after the test developers to show equivalent between the two platforms or if there are any specific areas of concern to support a system on both platforms?

What we've seen is there may be significant differences in the code base in order to produce equivalent performance. Do you have any thoughts on what studies are required to support their equivalency?

Dr. Timothy Stenzel: So the test is a serology test or an antigen test, a molecular test?

(Joann Gonzales): It's a rapid antigen...

Dr. Timothy Stenzel: Rapid antigen?

(Joann Gonzales): Using a mobile medical app.

Dr. Timothy Stenzel: Okay and that app will read the results of the test or will it...

(Joann Gonzales): It'll...

Dr. Timothy Stenzel: ...just be an app for reporting function not involved with reading the results of the test or, you know,?

(Joann Gonzales): It will involve - it will provide step-by-step instructions. And then it will also capture the image and provide results and will have the function for reporting also.

Dr. Timothy Stenzel: So it's capturing the image and is it based on that image is it making the assessment of whether it's positive or negative or indeterminate?

(Joann Gonzales): Correct.

Dr. Timothy Stenzel: Okay. So that obviously cell phones are different even within a family, you know, iOS or Android, the different models are available and have different cameras, different resolutions. Lighting may play a big role exactly how you hold something. And that could have differences between even within a family of cell phones models.

So it's best if there is a study showing equivalency between those. They don't have to be on actual patient samples. So you could validate with say with one model or you could validate with any of the models that you would accept in the study of home users. But then show basically with analytical work that

there's, you know, with high, medium and low positive samples and different lighting conditions, that the different models, you know, perform equivalently and which ones don't.

So there's a great deal of flexibility here. And so the best thing to do is to propose a study design however you want to run your study and then how you would propose to validate the different models that you would allow in the authorization. But we do think that in the labeling the models that you've validated should be stated and that, you know, obviously performance outside of that would not be known.

(Joann Gonzales): Okay. Thank you very much.

Coordinator: Thank you. Our next question is from (Roxanne Chan). Your line is open.

(Roxanne Chan): Thank you for taking my call. Regarding a multi-analyte molecular test validation with clinical samples we understand the need of using an FDA cleared comparator assay for flu A and B. Does FDA have any guidance on say the - how recent these FDA cleared comparative assays we should use?

And also given the flu rate is so low we only have access to archived flu samples. Does FDA have any guidance on the age and the storage conditions of these archived samples to be applicable in clinical validation?

Dr. Timothy Stenzel: Okay please stay on the line because I want to make sure I've unpacked all of that question because there's quite a bit. Let's talk about banked samples, you can use banked samples. We do ask that you support through stability studies the use of say the oldest of those samples but there's no problem using banked samples for the non-SARS target.

(Roxanne Chan): Okay.

Dr. Timothy Stenzel: There will be a post-market commitment to do a prospective study for those analytes but we understand that especially flu, there's very little flu circulating so bank sample is really the only way that you're going to be able to assess that.

I'm not aware of any limitations on the authorized comparator test for non-SARS targets. As long as it's FDA authorized molecular test that would be acceptable to us.

(Roxanne Chan): Fantastic. Thank you very much.

Coordinator: Thank you. Our next question is from (Ron Domingo). Your line is open sir.

(Ron Domingo): Thanks Tim and Toby. My question has two scenarios. So what is the agency's view on software changes that improve performance in the context of the pandemic? So in this one scenario after authorization the developer finds a way to improve the algorithm and it does increase the PPA from 90% to 92% without any changes in usability.

Based on the guidance, FDA guidance deciding when to submit a 510(k) for a software change to an existing device this would require a new 510(k) since it has a direct impact on diagnostic performance. Would a similar rationale apply here to an EUA? So would we require a new EUA or EUA amendment?

Dr. Timothy Stenzel: So it depends. So we are encouraging developers if they know they're going to make software modifications that may alter the performance and hopefully improve performance or you just don't know if it's going to alter the performance but you're planning on doing it, that during the EUA process

that you secure from the FDA sort of preapproval of preauthorization of a change or modification which would include covering the kinds of changes you would make and how you would assess performance and what would represent an adequate performance acceptable after you evaluate the change.

And if that is built into your authorization then if everything looks great and it meets everything that the FDA and the developer expected to see there would be no need to come in for a modified change unless there would be an updated labeling, anything, any different instructions or if you wanted to actually show that you have better performance and modify the data in your EUA authorization to show that your test is now more sensitive.

If you had not - if you already have in EUA authorization and you have not preset that change modification procedure then we yes, we'd want to see the data as an amendment. Now if you - if this is a point of care or a home test we would need to see that data and review it and reauthorize prior to launching that.

However if you have a kit for use in high complexity labs you can validate that, submit the validation to us and immediately launch that change while we review it and prior to making...

(Ron Domingo): Okay thanks.

Dr. Timothy Stenzel: ...the EUA authorization decision.

(Ron Domingo): Okay yes, thank you. Yes I was going to ask the second scenario but your response was very thorough. Thank you Tim.

Dr. Timothy Stenzel: You're welcome thanks.

Coordinator: Thank you. Our next question is from (Karen Gerard). Your line is open.

(Karen Gerard): Hi. Thank you for taking my call. Earlier in the pandemic the FDA allowed for enrichment due to low prevalence but not long ago we had peak prevalence that allowed for very quick enrollment of both symptomatic and asymptomatic subjects in prospective clinical trials. The current rates are dropping though.

So my question is specifically for molecular tests what does FDA think about recruiting subjects that have had a positive antigen or PCR test in the past 48 hours?

Dr. Timothy Stenzel: Yes so this is something probably we want to take a look at prior to you starting this study if you don't want to have the study be at risk. But definitely I have publicly stated for accumulating multiple times I think on this town hall call and other settings as well that for enriching for asymptomatic individuals you can connect with some sort of regular testing program. And if they're positive then you can resample and use it in your test.

We just want to know that design, when you do that we also of course want to see that you keep everybody blinded to the prior results and include at least equal number of negative results in that blinded retesting. So if somebody gets the test, they're negative then we would want a portion of them included as well as the portion, you know, that you need to get to the recommended number of positives for the study.

(Karen Gerard): Okay. Thank you very much.

Coordinator: Thank you. Our next question is from (Kadumi Venkat). Your line is open sir.

(Kadumi Venkat Shuran): Thank you for taking the call. I am (Kadumi Venkat Shuran) from Tetracore. I wanted to ask about the serology test and especially now the vaccinations are there - the differentiation of vaccinations whether it's infection through serology. I think the last meeting you mentioned that probably for test such a test comes there that's a higher priority.

Earlier when you were mentioning that was not discussed. So can you please elaborate still if for serology test that comes to differentiate vaccination whether the infection is it of interest to the agency? Thank you.

Dr. Timothy Stenzel: Yes. If the application is complete and has evidence that could support such a claim, then we will make that review a high priority. The study designs for supporting such use so are not insignificant and so just look at that. And you probably want to run an SOP, a study design SOP by the FDA to see if that is going to support whatever claim that you may seek.

(Kadumi Venkat Shuran): Thank you.

Coordinator: Thank you. Our next question is from (Annie Bell). Your line is open.

(Annie Bell): Hi there. Can you hear me? Hello?

Dr. Timothy Stenzel: Yes.

(Annie Bell): Okay great, thanks.

Dr. Timothy Stenzel: Yes we can hear you.

(Annie Bell): So we're - I'm - I have a two-part question in regards to the antigen template. So there's a request to do 35 - or 30 positive, 30 negative and then that could be retrospectively collected samples and then five positives prospectively collected samples that are not in transport media. I'm just wondering how FDA is assessing the success of those five positives that aren't in transport media? That's one part of the question.

Dr. Timothy Stenzel: Yes, we'll of course we'll...

(Annie Bell): Yes.

Dr. Timothy Stenzel: Yes, we'll look at all the data and make an assessment. Obviously if they're all negative that would be a problem, right? So the other thing just to fill out the responses, you know, getting negatives is really easy so we'd like to see all the negatives fresh. But you can enrich 25 of those 30 with bank samples.

We know that in some cases freezing samples releases more target and actually may improve the sensitivity of the assay. So we would definitely like to see that there is no significant drop in sensitivity. But we look at all the data and we make the assessment based on the data that's presented and the best - and using the best good science to evaluate it.

(Annie Bell): Okay and then the second part is the template notes that some can be collected post authorization. So are the five prospective positives included in that post authorization collection?

Dr. Timothy Stenzel: Yes so if you did five fresh and 25 banked post market, you know, everything else being equal an average submission we would, you know, no

outstanding concerns, we would ask for just 25 more fresh samples post market.

(Annie Bell): Okay so what if our - what if 25 banked and five prospective?

Dr. Timothy Stenzel: So if there are five - 25 banked and five fresh?

(Annie Bell): Yes.

Dr. Timothy Stenzel: Yes, so you - so we want to see complete data ultimately on 30 - a minimum of 30 fresh samples. So whatever you don't contribute to that 30 in the premarket, preauthorization base we would like to see in the post - in the post market study.

(Annie Bell): Okay thank you.

Dr. Timothy Stenzel: So we want to see a total of 30 fresh results but we are allowing pre-market the enrichment with banked in order to aid in getting particularly point of care tests onto the market as soon as possible in...

(Annie Bell): And those 30 fresh results can...

Dr. Timothy Stenzel: ... yes.

(Annie Bell): Oh, sorry to interrupt.

Dr. Timothy Stenzel: Okay, no what's the question?

(Annie Bell): But those 30 fresh results...

Dr. Timothy Stenzel: Yes, go ahead.

(Annie Bell): ...can be a mixture of positive and negatives correct?

Dr. Timothy Stenzel: No, no. No we want to see per application for a point of care test we want to see a minimum of 30 overall fresh positives. So you can - if you only do five fresh positives pre-market we would want to see five fresh positives, 25 fresh positives post market.

(Annie Bell): Okay. Thanks for the clarification.

Toby Lowe: And to clarify I believe the template also recommends 30 banked - so we want at least 30 of a complete data set where there - if there's - if your premarket is using banked, we want 30 banked even if you have five additional fresh on top of that.

Dr. Timothy Stenzel: You're right Toby - I - you're right. Thanks for correcting me. What we want to see is for the bank that could be frozen direct swabs or it can be frozen in VTM. We want to see a complete set of data for that sample type, that frozen sample type in order to make our premarket decision. And we want to make sure with the fresh positives that the test performance is still holding up.

(Annie Bell): Understood. Okay thank you.

Coordinator: Thank you. Our next question is from (Shuru Romkular). Your line is open.

Dr. Timothy Stenzel: Hello?

(Shuru Romkular): Hello? Hello?

Toby Lowe: Yes we can hear you.

Dr. Timothy Stenzel: We can hear you yes.

(Shuru Romkular): Hi, sorry. So the first part of my question is that if a manufacturer has a legally marketed device and they want to add a COVID-19 diagnostic to that device, I just want to clarify that the information required for the EUA request would be limited to the validation of the assay itself and we wouldn't need to provide technical information on the device if it's unchanged.

And the second question is that if you're submitting EUA for a COVID-19 assay on a market device can you now apply this assay to additional instruments of the same instrument family under the replacement reagent policy in the same way as a 510(k) cleared assay would be?

Dr. Timothy Stenzel: So can you tell me a little bit more details about your assay? Is this a molecular panel you're adding SARS-CoV-2 to other respiratory or what is this, you know, what are the non-COVID targets on this assay and what is it doing?

(Shuru Romkular): So it's basically looking at a marker for seriousness of COVID-19 infection so say like a cytokine?

Dr. Timothy Stenzel: Oh, so okay well, you know, we've authorized some IL-6 assays. I'm not sure other than IL-6 what we've done hasn't been either serology antigen or molecular including panels of respiratory viruses.

I think this is specific enough that you ought to come with, you know, a pre-EUA with what you plan on doing to add that because it doesn't sound like you're adding a SARS test to a, you know, a SARS either serology or a

diagnostic to for identification of the virus or exposure of the virus to another serology or direct test.

So it sounds like you have inflammatory markers for some other purpose and you want to add a COVID-19 related inflammatory marker or something to your - or, you know, apply for the use of your device for a COVID-19. And so that is a - going to be a little bit more unique and will depend on your given panel.

In general when you're adding something to the panel depending on how that panel works if the wells are all independent and there's no, you know, there's no change in those independent wells and you're just adding a new well for SARS or wells for SARS and it has no direct impact on the other wells, then that is going to really make it a more streamlined to validate the addition of those new marker - that new marker or markers because what you're adding doesn't impact the results of the other markers of the analytical result in the other markers.

On the other hand if there's some sort of, you know, everything together and you're adding SARS probes into already a mix that adding that into the mix could alter the performance of the other marker. So I really recommend that you just write up your idea and send it in as a pre-EUA. And that will be and likely go to one of our ancillary COVID teams that would review this type of application. It doesn't go in with the regular mix of serology antigen or molecular.

(Shuru Romkular): Okay but I think, you know, just to clarify it's basically there's a device that's say already 510(k) cleared for some other purpose and my question is now I want to add a - some kind of cytokine assay to this device and so, you

know, I'm only asking if the information that I can provide is related to the validation of the assay and not the instrument?

Dr. Timothy Stenzel: Yes and what I'm saying is without unique details to your platform I can't give you any more specific information today.

(Shuru Romkular): Okay. All right thanks.

Coordinator: Thank you. Our next question is from (Lynn Ko). Your line is open.

(Lynn Ko): Hi. I actually think someone earlier mostly answered my question but maybe I'll just ask a clarifying question about something you said earlier Tim. And it was around just comparison in iOS and Android and specifically just around, you know, different code bases that might be required to basically produce an equivalent off one of those platforms.

It sounds like from your answer previously that ultimately it's the device equivalently data that is most important to the agency. Is that correct and essentially it doesn't really matter how you get there so long as the data approved equivalents or do we just skip over that part of the question?

Dr. Timothy Stenzel: Yes I mean I don't know how you would carry out the clinical study portion of this for the users whether you would allow any of their devices to be used or whether you're going to use one specific device in those studies. And, you know, it might be better to have multiple. Whatever the patients have as a device you use that and you look at the overall performance.

Separate from that we would, because you may only get one result from an Android this model X and whatever and only one result from an iOS model seven. So we want to know more data about the comparative performance if

it's actually doing the reading of the test and making the reading results available to the patient.

And obviously there as we discussed before there could be different - they could yield different performance measures based on the fact that the algorithms might be different, and cameras might be different, the resolutions might be different.

The background lighting conditions maybe - they may be less or more sensitive to that. The other thing I thought about it is there's all sorts of modes of taken a picture with a smart phone, you know, the essentially portrait, and landscape and, you know, night and day and all those things can, you know, potentially impact the accurate reading of the result. We just want to make sure that whatever, you know, you're going to put in your labeling that they're all going to be accurate results.

(Lynn Ko): Good, great. Thanks for the clarification.

Coordinator: Thank you. Our next question is from (Elaine Allen). Your line is open.

(Elaine Allen): Hi. thank you. My question is this. If we want to sell a diagnostic test for COVID-19 while the EUA request is still pending FDA review and the EUA were to be rejected I understand we would need to call any distributed test. However what would be the impact to the patient samples that have already been tested? Are those still valid?

Dr. Timothy Stenzel: And Toby can I ask you to answer that question?

Toby Lowe: Yes absolutely.

Dr. Timothy Stenzel: And unfortunately this week again I'm going have to leave a little early, apologies but you're in good hands with Toby. Thank you.

(Elaine Allen): Yes thank you very much.

Toby Lowe: Thanks Tim. And just to make sure that I caught your question you're asking about if you submit an EUA request concurrently with a 510(k)?

(Elaine Allen): No, no, no we were submitting an EUA request for a diagnostic for COVID-19. It's, you know, we're under the notification so we're distributing the tests. That should the EUA request be denied or rejected? Now we've distributed tests and of course I understand we have to recall any distributed tests but what would be the impact of the patient samples who have already been tested? Are they still considered to be valid?

Toby Lowe: Got it. I'm glad I asked for that clarification since I had missed that nuance there. That is something that we would work with you as we concluded our review and went to a denial.

We would work with you depending on the impact of the incorrect or sorry, of the reported results whether we expected you to do a communication to all your clients or were to send out corrected test results or, you know, invalidated test results or there anything like that, it would depend on the specific circumstances and we would work directly with you on that.

(Elaine Allen): Okay so if I understand just for clarification it would - there would be a some sort of an rejection agreement need? Within that rejection agreement it would be outlined what would be necessary whether contact customers at present - have perform testing and what we may need to do as a result of that?

Toby Lowe: Right. It wouldn't necessarily be part of the denial but it would be something that we would work with you on after a denial decision was made.

(Elaine Allen): Okay. And so there's no - so it would just - it depends right?

Toby Lowe: Right, right exactly, always the best answer right?

(Elaine Allen): Yes. Well then the project team's going to love hearing that but thank you very much. I appreciate it Toby.

Toby Lowe: No problem.

Coordinator: Thank you. Our next question is from (Esther Yen). Your line is open.

(Esther Yen): Thank you. Yes my question is simple. Back to the new guidance document, I'm not sure how proscriptive that document might be but as it relates to a mutant genotype detection or confirmation is there a minimum number of samples that are required to make that call? Hello?

Toby Lowe: Sorry I forgot to take myself off mute there. So I'm trying to think through the, the specifics of the guidance. And I don't believe that it gets into that level of detail, but that is something that you could come in with a proposal regarding.

(Esther Yen): So with the pre-sub? Okay.

Toby Lowe: Yes. Yes.

(Esther Yen): And related question in the sample stability testing, are you required to use just the natural samples only or can we supplement some with the contrived samples?

Toby Lowe: Sorry that was regarding sample stability?

(Esther Yen): Correct stability testing.

Toby Lowe: I would have to look at the template to see what is recommended there. Let me see if I find that very quickly and if not I will ask you to send that in. Okay I believe that you can use inactivated virus for sample stability.

(Esther Yen): Thank you.

Toby Lowe: Yes.

Coordinator: Thank you. Our next question is from (Laura Ferguson). Your line is open.

(Laura Ferguson): Hello. Thanks for taking my call. I wanted to know what the cut off is or what the order of magnitude was being referred to with regard to laboratory tests being considered high priority for I believe the term Tim used was significantly high throughput. What level of throughput is that?

Toby Lowe: Thanks for that question. I believe Tim addressed this a little bit last week on the call as well. We don't have a firm number that we've put out because this does change a little bit depending on other details such as, you know, submissions in-house and as the pandemic progresses.

So if you do have a specific question for your test and want them to know whether it would be considered high throughput or significantly high throughput you can send that in through the mailbox and we can take a look.

(Laura Ferguson): Okay thank you.

Coordinator: Thank you. Our next question is from (Shannon Clark). Your line is open.

(Shannon Clark): Hello. This is (Shannon Clark). So my question is in relation, with UserWise. This question is in relation to antigen point of care studies The antigen kind of footnotes point of care studies should be run in the United States.

And to obtain point-of-care use of an antigen test kit can you run the point-of-care study in Brazil with Brazilian healthcare professionals if we submit a justification of equivalency between the Brazilian healthcare providers and the US healthcare providers? And as part of this can we translate the point-of-care instructions in the Portuguese via a certified translator and still use a study such as this?

Toby Lowe: So we definitely recommend that these studies be conducted in the US because we do - we have seen differences between populations in, you know, in the US and other countries specifically with how, you know, practice of medicine and how healthcare providers are trained, et cetera.

If you have a proposal specific to your situation that you'd like us to consider we always consider alternate proposals and you can send that in. But we highly recommend that you do that in advance of starting a new study in case we do not agree with the proposal.

(Shannon Clark): And can I submit a study synopsis rather than the full protocol in order to get clarity sooner or do you require a full clinical evaluation protocol?

Toby Lowe: You can submit the synopsis. It is it's quite likely that we would request additional details as we take a look so...

(Shannon Clark): Okay thank you so much.

Toby Lowe: Sure.

Coordinator: Thank you. Our next question is from (Sue). Your line is open.

(Sue): Hi Toby. Thanks for taking my question. I think part of this was already answered and don't want to belabor this. It was around the antigen performance and the five prospective samples. I just want to know if you could clarify so the samples could be collected retrospectively or prospectively but then in addition the submission would need to include those five prospective samples without transport media and then while you're continuing to get the 30 positives throughout.

And then I am just looking at a recent IFU that was just published I think this week where it's intended for fresh samples but the clinical performance is all on banked samples, all unfrozen samples so I was just curious if you could talk a little bit about that?

Toby Lowe: Right so we would want to see a complete data set of 30 specimens. Without knowing exactly which test you're referring to I can't comment on the ISU but we would want to see, you know, complete data set of 30. And then if you have additional fresh that would be on top of the 30 and we would ask for the rest of the 30 fresh to be in the post authorization.

(Shannon Clark): Okay. Okay great. Thank you.

Coordinator: Thank you. Our next question is from Debs Payne. Your line is open.

Debs Payne: Hi. Thank you for taking my call. This is Debs Payne, PDP Consulting. And we're interested in exploring, validating a mouthwash collection alternative collection type on our to amend our submitted EUA that is using nasal swabs.

I had reached out to the templates email and they had told me to contact my primary reviewer. But it's been seven months and we don't have a primary reviewer for our EUA so I'm seeking guidance on what that might look like, what that validation might look like.

Toby Lowe: Okay. So I would start by recommending that you take a look at the alternate specimen type validation information in the template. That would be a good starting point. And then if that does not seem like it is applicable to...

Debs Payne: I think...

Toby Lowe: ...the situation you can submit the question again through the mailbox and just flag that you don't have a lead reviewer and so you would like to get some input. And if you want to direct that or ask that they include me on that email you can do that and they will flag it for me.

Debs Payne: And how - what is your email address?

Toby Lowe: Or you can just send it to the EUA mailbox and they'll add it - they'll forward it to me.

Debs Payne: Okay because I think if you have an alternate one for saliva but the mouthwash is quite different.

Toby Lowe: Right. That's why I suggested taking a look at that alternate specimen which your right, it's for saliva to see if that information is applicable and then if you have additional questions...

Debs Payne: Okay.

Toby Lowe: ...on top of that you can send them in.

Debs Payne: Thank you. You all are doing a good job. I'm hoping to get a response from a reviewer one day but patience is a virtue.

Toby Lowe: Thank you for understanding.

Debs Payne: Okay thank you.

Toby Lowe: Sure.

Coordinator: Thank you. Our next question is from (Nisha Lee). Your line is open.

(Nisha Lee): Hi. Thank you for taking my call. My question is regarding the variant testing and our company's developing a POC antigen test. So we've looked to places like BEI and have been an excess - successful in obtaining inactivated virus.

So my question is, is it acceptable to FDA that we run an in silico analysis on the protein alignments of the nuclear protein from each variant and mapped it against our anti-body actuals because idea is that if our actuals do not map

near these regions then we would have very low risk of seeing a decrease in our performance.

Toby Lowe: And I'm sorry what type of test is this for?

(Nisha Lee): Oh this is for a POC antigen test.

Toby Lowe: For antigen okay. I wasn't sure...

(Nisha Lee): Yes.

Toby Lowe: ...if there was antigen or serology there. Is that something that is probably - it would probably be best if you can send in your proposed plan and we can take a look at it and get you some feedback.

(Nisha Lee): Okay thank you.

Irene Aihie: Thank you. Thank you so much Toby. I believe you wanted to make a clarification. That was in fact our last question. So you can go ahead and clarify.

Toby Lowe: Great thank you Irene. I just wanted to jump back to a question that we had earlier in the call about enrichment due to reduced positivity rates. Tim did address this a little bit with talking about, you know, the potential downfalls of enrichment but we just wanted to clarify that enrichment - enriching your study with known positives can cause bias.

So we would expect your study design to include a plan for addressing that bias. So just wanted to jump back to that topic and make that clarification in case that I wasn't clear in the previous remarks.

And that's all for today I think. I'll turn it back over to you Irene.

Irene Aihie: Thank you so much. Thank you. This is Irene Aihie. We appreciate your participation and thoughtful questions during today's town hall. Today's presentation and transcript will be made available on the CDRH learn Web page at www.fda.gov/training/cdrhlearn by Friday, March 5. If you have additional questions about today's presentation please email cdrh-eua-templates@fda.hhs.gov.

As we continue to hold these virtual town halls please we would appreciate your feedback. Following the conclusion of today's virtual town hall please complete a short 13 question survey about your FDA CDRH virtual town hall experience. The survey can be found at www.fda.gov/cdrhwebinar. Again thank you for participating and this concludes today's virtual town hall.

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